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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,418	09/26/2003	Michelle Prudhomme	SERVIER 411	8444

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EXAMINER	
ANDERSON, REBECCA L	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 02/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/672,418	PRUDHOMME ET AL.	
	Examiner	Art Unit	
	Rebecca L. Anderson	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-40* is/are pending in the application.

4a) Of the above claim(s) *39* is/are withdrawn from consideration.

5)☒ Claim(s) *21-24 and 31-38* is/are allowed.

6)☒ Claim(s) *25-30 and 40* is/are rejected.

7)☒ Claim(s) *25-30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 21-40 are currently pending in the instant application. Claims 21-24 and 31-38 appear allowable over the prior art of record. Claim 39 is withdrawn from consideration as being for non-elected subject matter. Claims 25-30 are objected. Claims 25-30 and 40 are rejected.

Election/Restrictions

Applicant's election with traverse of Group I, claims 21-38 and 40, in the reply filed on 22 November 2005 is acknowledged. The traversal is on the ground(s) that a chemist would not find the invention to involve structurally distinct inventions and that there is no basis for a restriction between the methods and the products. This is not found persuasive because inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. In the instant case, the product as claimed can be used in a materially different process of using that product as can be seen by the instant specification, see page 45, wherein the product of the invention can be used for the treatment of different diseases such as lung carcinoma or prostate carcinoma.

However, the requirement for the election of a specific compound, found on page 3 of the restriction requirement mailed 25 October 2005, is withdrawn.

Therefore, **the elected invention for search and examination is**: the products of the formula (I) as found in claims 21-38 and 40.

The requirement is still deemed proper.

Claim Objections

Claims 25-30 are objected to because of the following informalities: the claims do not contain a period at the end of each claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 40 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pharmaceutical compositions useful in treating lung carcinoma and prostate carcinoma, does not reasonably provide enablement for the treatment of all cancers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,

3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, claims:

The nature of the invention

The nature of the invention is pharmaceutical compositions useful in treating cancer comprising as active principle an effective amount of a compound of claim 21, together with one or more pharmaceutically acceptable excipients or vehicles.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:
It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since as the state of the prior art is that cancer

therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al. page 531) Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them. It is also known in the prior art (Lala et al. page 91) that the role of NO in tumor biology remains incompletely understood with both the promotion and inhibition of NO mentioned for the treatment of tumor progression and only certain human cancers may be treated by selected NO-blocking drugs. These example shows that there are different cellular mechanisms, the unpredictability in the art and the different treatment protocols.

Hence, one of skill in the art is unable to fully predict possible results from the administration of the compound of the claims since various types of cancers have different causative agents, involve different cellular mechanisms and differ in treatment protocol.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the specification is the generic discussion on page 1 that the compounds of the invention are useful in the treatment of

cancers, for example, adenocarcinomas, carcinomas, sarcomas, gliomas and leukaemias. The only data found in the specification, which provides enablement for the treatment of lung carcinoma and prostate carcinoma, is in vitro activity for three cell lines with the compound of example 2 on pages 45-46. There are no working examples present for the treatment of any type of cancer.

The breadth of the claims

The breadth of the claims is a pharmaceutical composition for the treatment of any cancer.

The quantity of experimentation needed and the level of the skill in the art

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what cancers out of all cancers would be benefited (treated) by the administration of the pharmaceutical composition of the claim and would furthermore then have to determine which of the claimed compounds would provide treatment of which cancer, if any.

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad intended use of the pharmaceutical composition of the instant claim for the treatment of any cancer. As a result necessitating one of skill to perform an exhaustive search for which

cancers can be treated by what pharmaceutical compositions of the instant claim in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which cancers can be treated by the pharmaceutical composition encompassed in the instant claim, with no assurance of success.

This rejection can be overcome by deleting the intended use from the claim.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically claims 25-30 are claiming compounds of claim 21 which are (IA), (IB), (IC), ID), (IE) and (IF). However, the variables (i.e. Z, W1, R1, R2, R'2, Rb, Rc, Rd, Re) on the compounds (IA)-(IF) are not defined in the claims 25-30 and it is unclear what the definitions of these variables include, i.e. are they defined as found in claim 21, are they defined to include substituents outside of the

scope of the variables in claim 21 or are they defined to be further limiting than the variables in claim 21. It is suggested that applicant amend the claims to include the definitions of the variables on formulas (IA)-(IF) or, if the variables are as defined in claim 21, add the statement, for example, "wherein Z, W1, R1, R2 and R'2 are as defined in claim 21".

Closest Prior Art

Claims 21-24 and 31-37 appear allowable over the prior art of record. The closest prior art or record is Bergman et al., which discloses the compounds 13-16 on page 2616 which are the compounds present in applicants' instant proviso of claim 21. The prior art reference of Bergman et al. does not disclose any utility for the compounds 13-16 and fails to provide any direction or motivation to modify the prior art compounds to arrive at applicants' instantly claimed compounds.

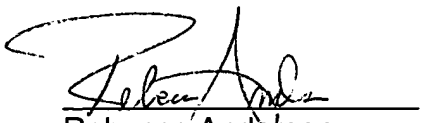
Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



February 9, 2006

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